REMARKS

Claims 1, 2, 5-7 and 9-33 are pending in the application. Claims 12-27 are withdrawn from consideration as being drawn to a non-elected invention. Claims 3-4 and 8 were previously canceled without prejudice or disclaimer. Claims 2, 9, 10 and 30-31 are now canceled without prejudice or disclaimer. Claims 1, 7, 11, 32 and 33 have been amended to better clarify what Applicants regard as the invention. Support for the amendments can be found throughout the specification, but particularly in original claims 9-11. Further support may be found in the specification on page 26, paragraphs [0088] and [0089] and in Figure 5. No new matter has been added by way of this amendment. Thus, as a result of the foregoing amendment, claims 1, 5-7, 11, 28-29 and 32-33 are under consideration. Reconsideration of this application is respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph

By way of this Action, the Examiner has rejected claims 1, 5-7, 9-11, 28-30, 32 and 33 under 35 U.S.C. §112, first paragraph for lack of enablement. In particular, the Examiner alleges that while being enabling for an isolated glycosylated endopeptidase that is isolated from a Streptococcus or a Staphylococcus bacterium, having a pH optimum between 7.5 and 10, an apparent molecular weight of 14,000 Da, and cleaves at the glutamic acid at position 9 and after the serine at position 6 of SEQ ID NO: 2, does not reasonably provide enablement for said isolated glycosylated endopeptidase that is isolated from a Streptococcus or a Staphylococcus bacterium having said pH optimum and molecular weight properties that cleaves at a site within, or C-terminal to the LPXTG motif (SEQ ID NO: 1; the cleavage limitations recited in instant claim 1) or the ability to bind and cleave a substrate containing an amino acid sequence comprising LPXTG motif (SEQ ID NO: 1; the limitations pertaining to cleavage specificity of claims 30 and 33). The Examiner alleges that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

More particularly, the Examiner alleges that claim 1 recites that the endopeptidase cleaves at a site within, or C-terminal to the LPXTG motif (SEQ ID NO: 1) and claims 30 and 33 recite a broader cleavage specificity wherein the endopeptidase binds and cleaves a substrate containing an amino acid sequence comprising LPXTG motif (SEQ ID NO: 1).

However, the Examiner alleges that the specification discloses that the cleavage specificity of the claimed endopeptidase is much narrower than claimed in the independent claims 1, 30 and 33. For example, Example 1 (pages 25-26) discloses that the non-immobilized synthetic peptide of SEQ ID NO: 2, KRQLPSTGETANPFY, was cleaved by the endopeptidase at two sites, after the serine at position 6 and the glutamic acid at position 9, whereas the endopeptidase cleaved only after the glutamic acid at position 9 in the bound form SEQ ID NO: 2. The Examiner notes that it is assumed that the endopeptidase was blocked by the bead to which the polypeptide was immobilized and, therefore, unable to cleave after position 6. The specification further discloses that the endopeptidase did not cleave reversed or random peptides having the LPSTG sequence or BSA. Therefore, the Examiner alleges that the specification discloses that the specificity of the endopeptidase is much narrower than claimed.

The Examiner further alleges that the limited showing of cleavage specificities that are limited to certain positions in a particular polypeptide is not sufficient to enable a claim drawn to an endopeptidase that cleaves within a motif defined as LPXGT or C-terminal thereto or an endopeptidase that binds and cleaves a substrate anywhere as long as the substrate contains the LPXGT motif because the art of Enzymology is too unpredictable.

The Examiner notes that with the exception of the cleavage specificity of the non-immobilized SEQ ID NO: 2; the specification fails to guide the skilled artisan as to the particular structural and conformational characteristics of other polypeptide substrates that can be cleaved by the claimed endopeptidase with a reasonable expectation of success.

The Examiner alleges that there is no predictable way for a skilled artisan to know in advance what other polypeptides having the LPXGT motif, in addition to SEQ ID NO: 2, can be cleaved by the endopeptidase as set forth in the instant application and that it would require one of ordinary skill in the art undue experimentation to predict what other polypeptides having the LPXGT motif, in addition to SEQ ID NO: 2, can be cleaved by the endopeptidase according to the directions of the instant disclosure. Thus, the Examiner alleges that claims 1, 5-7, 9-11, 28-30, 32 and 33 are not commensurate in scope with the enabling disclosure.

Applicants respectfully traverse the Examiner's rejection and have amended the claim to recite wherein the endopeptidase cleaves at the glutamic acid at position 9 and after the serine at position 6 of the SEQ ID NO: 2. In particular, claim 1 recites:

> *"An isolated, glycosylated endopeptidase enzyme, wherein said enzyme is isolated from a Streptococcus or a Staphylococcus bacterium, and is characterized as having a pH optimum between 7.5 and 10, an apparent molecular weight of 14,000 Da, and is further characterized as cleaving after the serine at position 6 of SEQ ID NO: 2 and after the glutamic acid at position 9 of SEQ ID NO: 2 wherein said sequence contains a Leu Pro Xaa Thr Glu (LPXTG) motif which is present in a cell surface virulence factor of said bacterium, and wherein the enzyme is further characterized as containing carbohydrates essential for enzyme activity, wherein said carbohydrates are selected from the group consisting of L-fucose, D-galactose, D-galactosamine, D-glucose, D-glucosamine, and D-mannose."*

Moreover, claim 33 has been amended to recite:

"A glycosylated enzyme isolated from a Streptococcus or a Staphylococcus bacterium, wherein the enzyme is characterized as having the following characteristics:

- *a) a pH optimum between 7.5 and 10;*
- *b) an apparent molecular weight of 14,000 Daltons;*
- *c) having no cysteine or methionine;*
- *d) having no aromatic amino acids;*
- *e) being inhibited by hydroxylamine at a concentration of about 100 mM;*

f) having a backbone structure containing about 30% unknown amino acids;

g) having a Km of 0.26 mM when its substrate comprises the amino acid sequence of SEQ ID NO: 2;

h) cleaving a substrate containing an amino acid sequence comprising a LeuProXaaThrGlu (LPXTG) motif; wherein said substrate comprises the amino acid sequence of SEQ ID NOs: 2 or 3, and wherein the enzyme cleaves after the serine at position 6 of SEQ ID NO: 2, or after the serine at position 3 of SEQ ID NO: 3 and after the glutamic acid at position 9 of SEQ ID NO: 2; and

i) containing carbohydrates essential for enzyme activity, wherein said carbohydrates are selected from the group consisting of L-fucose, D-galactose, D-galactosamine, D-glucose, D-glucosamine, and D-mannose."

In addition, claims 9, 10 and 30 have been canceled, thereby rendering the rejection of these claims under 35 U.S.C. §112, moot. Furthermore, Applicants assert that the specification clearly provides enablement for the claims, as currently amended. As such, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 1, 2, 5-7, 9-11, 28, 29 and 33 under 35 U.S.C. §112, second paragraph, as being indefinite.

Regarding the phrase "enhanced virulence"

In particular, the Examiner alleges that the term "enhanced virulence" in claim 1 is a relative term which renders the claim indefinite, and that the term "enhanced virulence" is not defined by the claim, and that the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The Examiner further alleges that neither the claims nor the specification provide a comparison such that the ordinary artisan can ascertain to what the enhanced virulence is compared.

Applicants respectfully traverse the Examiner's rejection and have amended the claims to delete reference to the term "enhanced virulence" thereby rendering the rejection moot. Furthermore, claims 2 and 9-11 have been canceled, thereby rendering the rejection of these claims under 35 U.S.C. 112, second paragraph, moot.

Regarding "carbohydrates essential for enzyme activity"

In addition, the Examiner has rejected claims 1,30 and 33 under 35 U.S.C. 112, second paragraph as being incomplete for omitting essential structural cooperative relationship of elements, such omission amounting to a gap between the necessary structural connections. More particularly, the Examiner notes that claims 9-11 are drawn to carbohydrates that are "essential for enzyme activity" and that it is unclear why the limitations drawn to said essential carbohydrates do not appear in the independent claims since said carbohydrates are essential to the structure and activity of the enzyme.

While Applicants respectfully traverse the Examiner's rejection, Applicants have amended the claims to include the list of essential carbohydrates into the independent claims and have deleted the dependent claims containing this subject matter. As such, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. 112, second paragraph.

Regarding the phrase "having a KM of 0.26 mM"

The Examiner has also rejected claims 7 and 33 because the phrase "having a KM of 0.26 mM" is vague and indefinite because the measurement of a Michaelis-Menton constant, K_m, is specific for the substrate that is measured. The Examiner alleges that claims 7 and 33 do not specify what substrate is associated with the claimed K_m value.

While Applicants respectfully traverse the rejection, Applicants have amended the claims to recite that the substrate used for determination of the Km was the substrate of SEQ ID NO: 2. Support for this may be found in the specification on page 26, paragraphs [0088] and [0089] and in Figure 5.

Based on the foregoing, withdrawal of the rejections under 35 U.S.C. §112 first and second paragraphs is respectfully requested.

Fees

No fees are believed to be necessitated by the foregoing amendment and response. However, if this is in error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages.

Conclusion

Applicants believe that the foregoing amendments to the claims and arguments place the application in condition for allowance. Withdrawal of the rejections is respectfully requested. If a discussion with the undersigned will be of assistance in resolving any remaining issues, the Examiner is invited to telephone the undersigned at (201) 487-5800, ext. 129, to effect a resolution.

Respectfully submitted,

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